In the Specification:

Please replace the paragraph starting at page 2, line 21 of the substitute specification with the following paragraph:

--More specifically, it is an object of the present invention to provide compounds capable of interfering with the interaction between p53 and MDM2 and/or mdm2 in tumor cells having wild type p53, particularly human p53, and non-elevated MDM2 levels, as defined below, ~~*in vivos*~~ *in vivo* and *in vitro*. A preferred embodiment includes peptides and derivatives thereof, capable of binding to MDM2, particularly human DM2, and specifically exhibiting or blocking the binding of MDM2 to the p53 protein, particularly human p53, *in vitro* or *in vivo*. The preferred peptides of the invention are better than the ~~wildtype~~ wild type peptide in inhibiting the hdm2 binding to p53 or a suitable p53 peptide, as can be determined e.g. in suitable ELISA-type assays, particularly the assays described in detail hereinafter, on the basis of the IC_{50}, i.e. the concentration of peptide necessary to inhibit the hdm2 or p53 binding by 50%. The peptides of the invention mimic the MDM2 binding site on p53. The peptides provided herein consist of or comprise an amino acid motif (in N- or C-terminal order) of the formula

R_1-X-F-X-R_2-R_3-W-X-X-R_4 (I) SEQ ID NO: 4

wherein

R_1 is a proline (P), leucine (L), glutamic acid (E), cysteine (C) or glutamine (Q),
X stands for one (any) natural amino acid,
R_2 is arginine (R), histidine (H), glutamic acid (E), cysteine (C), serine (S), or preferably aspartic acid (D),
R_3 is histidine (H), phenylalanine (F) or preferably tyrosine (Y),
R_4 is phenylalanine (F), glutamine (Q) or preferably leucine (L); and
F and W (as well as the other capital letters given in brackets above) are used in accordance with the commonly used single letter code for amino acids and represent phenylalanine and tryptophan, respectively.--

Please replace the paragraph starting at page 15, line 24 with the following new paragraph:

--The method of the present invention encompasses ~~adm-inistering~~ administering DNA to tumor cells and/or a warm blooded animal, including a human. DNA of the present invention encodes a product that interferes with the interaction of p53 and MDM2. DNA typically is in an expression vector, such as a retrovirus, DNA virus or plasmid into which DNA sequences necessary for expression in eukaryotic cells are properly positioned to result in expression of the DNA. The DNA sequences are designed to express high levels of the desired product in tumor cells in a form that is stable and active as exemplified by the binding element TIP 12/1 described below. The DNA may be administered to cells ~~*in-vivos*~~ *in vivo*, ~~*ex-vivos*~~ *ex vivo* or *in vitro* as appropriate. The DNA may be administered encapsulated in liposomes, via microinjection or any other form known in the art to achieve efficient cellular uptake.--

Please replace the paragraph starting at page 16, line 4 with the following replacement paragraph:

-- Administering compounds that interfere with the interaction of p53 and MDM2 by affecting the expression of MDM2 are also encompassed by the method of the present invention. Triple strand-forming and antisense oligonucleotides which bind the mdm2 gene or its mRNA and prevent transcription or translation may also be administered to tumor cells and/or a warm blooded animal, including a human, ~~*in-vivos*~~ *in vivo*, ~~*ex-vivos*~~ *ex vivo* or *in vitro*. The oligonucleotides may interact with unprocessed mRNA or processed mRNA. Small molecules and peptides which specifically inhibit MDM2 expression may also be administered to cells.--

Please replace the paragraph starting at page 24, line 1, with the following replacement paragraph:

--Ac-Cys-Gly-Gln-Pro-Thr-Phe-Ser-Asp-Tyr-Trp-Lys-Leu-Leu-Pro-NH_2 (TFA salt) SEQ ID NO:~~33~~ 34 is obtained analogously to Example 1 (Mass spectral analysis (negative-ion mode):1694.7 (calc. 1695.0, $C_{80}H_{113}N_{18}O_{21}S_1$), t_R=8.39 (HPLC System A)). To a solution of Ac-

Cys-Gly-Gln-Pro-Thr-Phe-Ser-Asp-Tyr-Trp-Lys-Leu-Leu-Pro-NH_2 (18 μmol) SEQ ID NO: 34 in 20 ml of degassed phosphate buffer (pH=7.5) is added ~~6-acryloyl-2(dimethylamino)naphtalene~~ 6-acryloyl-2(dimethylamino)naphthalene (2-fold excess; Molecular Probes, Inc., Leiden, The Netherlands) dissolved in 2 ml of acetonitrile. The solution is stirred overnight at room temperature under an argon atmosphere. After completion of the reaction, 1 ml of trifluoroacetic acid is added and the solution is concentrated to dryness. The compound is purified by reversed-phase medium-pressure liquid chromatography.--

Please replace the table at page 35, after line 5 with the following new table:

--mdm2 binding site on human p53 PLSQETFSD L WKLLPENNV SEQ ID NO:1

phage clone 12/1	MPRFMDYWEGLN	SEQ ID NO: 6
phage clone 12/2	VQNF I DYWTQQF	SEQ ~~OD MP~~ ID NO: 63
phage clone 12/5	TGPAFTGYWATF	SEQ ID NO: 64
phage clone 15/1	IDRAPTFRDHWFALV	SEQ ID NO: 65
phage clone 15/5	PRPALVFADYWETLY	SEQ ID NO: 8
phage clone BB3	PAFSRFWSADLSAGAH	SEQ ID NO: 66
phage consensus	PXFXDYWXXL	SEQ ID NO: 3--

Please amend the paragraph starting at page 45, line 1 with the following replacement paragraph:

--In Vm.6 cells, having overexpressed MDM2, a positive response was observed when 3G5 antibody or TIP were injected intranuclearly. There was not a positive response ~~weht~~ when Trx was injected intranuclearly. 3G5 binds mdm2 within the p53 binding pocket thereby blocking p53-DMD2 association (Böttinger et al., 1997).--

Please amend page 45, line 5 as follows: ~~I~~

Please replace the paragraph starting at page 45, line 12 with the following replacement paragraph:

-- DNA encoding the described binding elements TIP 12/1, TIP wt and Trx and the pRGCΔFosLacZ reporter may be transiently transfected into the following three different cell types, OSA cells, a human osteosarcoma cell line-, U2-Os cells, another osteosarcoma cell line,

and MCF-7 cells, a breast ~~conacer~~ cancer cell line containing wild type p53. The OSA cell line contains a highly elevated mdm2 level due to gene amplification (Florence et al., 1994). The U2-OS cell line has no gene amplification for mdm2 but has elevated levels of dmd2-mRNA (Florence et al. 1994). The MCF-7 cell line contains heterogenously expressed low levels of wild type p53 and no reported mdm2 elevation.--